REMARKS

Claims 1 to 26, as amended, and new claims 29 and 30 appear in this application for the Examiner's review and consideration. Claims 27 and 28 have been canceled by this Amendment without prejudice to Applicants right to file one or more divisional or continuation applications directed to the subject matter of those claims. The new claims and the amendments are fully supported by the specification and claims as originally filed. In particular, the recitation of "in the absence of a tetrabutylammonium bromide catalyst" in the amended and new claims is supported at page 2, lines 7 and 8, of the present specification. Therefore, there is no issue of new matter.

Claims 2 and 25 were rejected as being anticipated allegedly by U.S. Patent No. 4,837,223 to Gobert et al. ("Gobert II") for the reasons set forth on pages 2 and 3 of the Office Action.

In response, Applicants submit that the presently claimed invention, as recited in claim 2, is directed to a process for preparing (S)-α-ethyl-2-oxo-1-pyrrolidineacetamide, i.e., levetiracetam. The claimed process comprises cyclizing (S)-N-[1-(aminocarbonyl)propyl]-4-chlorobutanamide, in a solvent selected from the group consisting of acetonitrile and methyl *tert*-butyl ether, in the presence of a strong base and the absence of a tetrabutylammonium bromide catalyst, and recovering the crude levetiracetam.

As recited in claim 25, the presently claimed invention is directed to crude levetiracetam, having a level of chemical impurities of less than about 0.2 percent, made by the process of the invention.

In contrast to the presently claimed method, Gobert II discloses, in claim 2, as cited in the Office Action, the preparation of (S)-alpha-ethyl-2-oxo-1-pyrrolidineacetamide, substantially free of (R)-alpha-ethyl-2-oxo-1-pyrrolidineacetamide, by cyclizing, in an inert solvent and in the presence of a basic substance, an (S)-2-amino-butanamide of the formula

$$X–CH_2CH_2–Y–NHCH(C_2H_5)CONH_2$$

in which X represents ZOOC– or $HalCH_2$–, wherein Z is alkyl of 1 to 4 carbon atoms, Hal is a halogen atom, and Y represents $–CH_2–$ or –CO–, with the proviso that Y is $–CH_2–$ when X represents ZOOC–, and Y is –CO– when X represents $HalCH_2$–. Gobert II does not disclose that the cyclizing process occurs in the absence of a tetrabutylammonium bromide catalyst, as presently claimed.

Gobert II also discloses that the cyclization is advantageously carried out in the presence of a catalyst of tetrabutylammonium bromide, and exemplifies the use of tetrabutylammonium bromide in the reaction. Column 2, lines 39 to 45, and Example 4, column 6, lines 15 to 26.

Moreover, Gobert II does not disclose that crude levetiracetam, having a level of chemical impurities of less than about 0.2 percent, as recited in claim 25, can be made using the method disclosed in that patent.

Therefore, Gobert II does not disclose cyclizing (S)-N-[1-(aminocarbonyl)propyl]-4-chlorobutanamide in the absence of a tetrabutylammonium bromide catalyst or a crude levetiracetam, having a level of chemical impurities of less than about 0.2 percent, and, thus, does not anticipate the present claims. Accordingly, it is respectfully requested that the Examiner withdraw the rejection of claims 2 and 25 under 35 U.S.C. § 102(b) over Gobert II.

Claims 1 and 7 to 21, were rejected under 35 U.S.C. § 103(a) as being unpatentable allegedly over U.S. Patent No. 4,696,943 to Gobert et al. ("Gobert I") for the reasons set forth on pages 4 to 10 of the Office Action.

In response, Applicants submit that, as recited in claim 1, the presently claimed invention is directed to a process for preparing (S)-α-ethyl-2-oxo-1-pyrrolidineacetamide (levetiracetam). The claimed process comprises reacting (S)-2-amino-butanamide hydrochloride and 4-chlorobutyryl chloride in a solvent selected from the group consisting of acetonitrile and methyl *tert*-butyl ether, in the presence of a strong base and the absence of a tetrabutylammonium bromide catalyst, and recovering the crude levetiracetam.

In contrast to the presently claimed invention, as stated in the Office Action, Gobert I discloses, at column 6, lines 3 to 32, using a tetrabutylammonium bromide catalyst in the reaction of (S)-2-amino-butanamide hydrochloride and 4-chlorobutyryl chloride, and, thus, does not disclose or suggest reacting (S)-2-amino-butanamide hydrochloride and 4-chlorobutyryl chloride in the absence of a tetrabutylammonium bromide catalyst, as presently claimed.

Therefore, as Gobert I does not disclose or suggest reacting (S)-2-amino-butanamide hydrochloride and 4-chlorobutyryl chloride in the absence of a tetrabutylammonium bromide catalyst, the claims are not obvious over that reference. Accordingly, it is respectfully requested that the Examiner withdraw the rejection of claims 1 and 7 to 21 over Gobert I.

Claims 26 to 28 were rejected under 35 U.S.C. § 103 as being unpatentable allegedly over Gobert II for the reasons set forth on pages 4 to 13 of the Office Action.

In response, Applicants submit that the presently claimed invention, as recited in claim 26, is directed to a pharmaceutical composition comprising the crude Levetiracetam recited in claim 25, which is made by the process of the invention, and has a level of chemical impurities of less than about 0.2 percent, and a pharmaceutically acceptable carrier; as recited in claim 27, the invention is directed to a pharmaceutical formulation comprising crude levetiracetam and a pharmaceutically acceptable carrier, wherein the formulation comprises less than 0.2% by weight of chemical impurities; and, as recited in claim 28, the invention is directed to the pharmaceutical formulation of claim 27, where the formulation comprises less than 0.1% by weight of chemical impurities.

As stated in the Office Action, at page 7, Gobert I discloses that, in the examples of that patent, the optical purity of the compounds obtained was verified by calorimetric determination of the differential enthalpies. The Office Action also states, at page 10, that Gobert II discloses that the disclosed compositions are substantially free of (R)-alpha-ethyl-2-oxo-1-pyrrolidineacetamide. However, Gobert I and Gobert II only make those references to optical purity cited in the Office Action, and do not disclose or suggest anything regarding the chemical purity of the disclosed compositions.

Thus, the cited references do not disclose or suggest crude levetiracetam, having a level of chemical impurities of less than about 0.2 percent, as presently claimed, or that crude levetiracetam, having a level of chemical impurities of less than about 0.2 percent, can be made with the methods disclosed in those patents. Therefore the cited references do not disclose or suggest the presently claimed invention.

Therefore, as the cited references do not disclose or suggest the presently claimed invention, the present claims are not obvious. Accordingly, it is respectfully requested that the examiner withdraw the rejection of claims 26 to 28 under 35 U.S.C. § 103(a).

Claims 8, 27, and 28, and claims 17 to 19 were rejected under 35 U.S.C. § 112, second paragraph, for the reasons set forth on page 13 of the Office Action.

In response, Applicants submit that claims 8, 27, and 28 have been amended to recite "% by weight of chemical impurities." In addition, claims 17 to 19 have been amended to correct the dependencies of those claims.

Therefore, the claims particularly point out and distinctly claim the subject matter Applicants regard as the invention, and, thus, meet the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, it is respectfully requested that the Examiner withdraw the rejections of claims 8, 27, and 28 and claims 17 to 19 under 35 U.S.C. § 112, second paragraph.

Finally, new claims 29 and 30 are directed to processes for preparing (S)-α-ethyl-2-oxo-1-pyrrolidineacetamide in the absence of a tetrabutylammonium bromide catalyst. Accordingly, the new claims are also patentable over the cited references.

Applicants thus submit that the entire application is now in condition for allowance, an early notice of which would be appreciated. Should the Examiner not agree with Applicants' position, a personal or telephonic interview is respectfully requested to discuss any remaining issues prior to the issuance of a further Office Action, and to expedite the allowance of the application.

The fees due for an extension of time and for one additional independent claim are believed to be $1020.00 and $200.00, respectively. Separate Extension-of-Time and Claim Fee sheets are attached. Please charge any additional fees that may be required to Deposit Account No. **11-0600**.

Respectfully submitted,

KENYON & KENYON

Dated: September 26, 2005

By: Alan P. Force

Alan P. Force
Reg. No. 39,673
One Broadway
New York, NY 10004
(212) 425-7200